Short Communication

Septic acute kidney injury in critically ill Indian patients

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Abstract

Acute kidney injury (AKI) is an independent variable for poor outcome in critically ill patients. The pathophysiology of septic AKI is distinct from that of non-septic AKI. We studied the clinical profile and outcome of septic AKI since such data is sparse in Indian patients. In this single-center retrospective, observational, cohort study, septic AKI has been found with high incidence (31%) and overall mortality was 52%. Age, number of non-renal organ failure, and APACHE II score were found as significant predictors of outcome in this population.

Keywords: Acute kidney injury, critically ill, intensive care unit, sepsis

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Introduction

Acute kidney injury (AKI) is a major concern in intensive care unit (ICU) patients, due to not only high incidence but also as an independent variable for poor outcome in these patients. The prevalence of AKI in critically ill patients had been reported to be varying from 1.5% to 70% depending upon the population studied and criteria used.[1-3]

The cause of AKI in critically ill patients is often multifactorial; sepsis being the most common.[1,4] Recent evidence suggests that AKI in patients with sepsis may have different pathophysiology including hyperemia, vasodilation, and acute tubular apoptosis instead of ischemia, vasoconstriction, or acute tubular necrosis.[5,6] In few small studies, clinical profile and outcome of septic AKI have differences when compared with non-septic AKI.[7-9] A large prospective observational cohort study of critically ill patients with AKI also showed that there was significant increased risk for death in patients with septic AKI.[10]

In the literature, there are as many as 35 different definitions of acute renal failure in critically ill patients being used. However, a uniform and precise operational definition of ARF was not available till recently. In 2004, the Acute Dialysis Quality Initiative (ADQI) has developed the RIFLE classification of AKI.[11] The acronym RIFLE defines 3 grades of increasing severity of ARF (risk, injury, and failure, respectively, R, I, and F) and 2 outcome variables (loss and end-stage kidney disease, respectively, L and E). A unique feature of the RIFLE classification is that, it provides for 3 grades of severity of renal dysfunction on the basis of a change in serum creatinine, reflecting changes in GFR or duration and severity of decline in urine output from the baseline. The RIFLE criteria have the advantage of providing diagnostic definitions for the stage, at which kidney injury still can be prevented (risk stratum), the one when the kidney has already been damaged (injury), and the one when renal failure is established (failure).

There are limited data from India on AKI in ICU patient population, which include both septic as well as non-septic AKI patients.[12,13] However, there is no available data from India focusing on septic AKI in

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critically ill patients. In view of the limited data on septic AKI and its likely importance, we sought to describe the clinical characteristics and predictors of outcome in critically ill patients with septic AKI.

Materials and Methods

This retrospective study of critically ill patients with septic AKI was performed in the department of critical care medicine at a tertiary care university hospital with a 1000 bed capacity. The department of critical care medicine has 12 beds ICU that caters to medical as well as surgical patients.

Sepsis was defined by the presence of both suspected or confirmed infection and at least 2 criteria of systemic inflammatory response syndrome, which includes abnormalities in temperature, heart rate, respiratory rate, or white blood cell count.[14] Acute kidney injury was defined by RIFLE criteria as described above. Septic AKI was defined by presence of AKI in patient with sepsis syndrome and also absence of other obvious cause that leads to AKI.

In this retrospective study, medical records of patients with septic AKI, who were admitted during the period of January 2006 to December 2008, were reviewed. Patients whose age was <18 years, with end stage renal disease or chronic kidney disease on maintenance hemodialysis, withdrawal of therapy during ICU stay, or incomplete data were not included in this study. Data were retrieved from individual case records of diagnosed septic AKI and were collected on a case report form. The form included age, gender, medical *vs*. surgical, primary source of infection, APACHE II score, RIFLE criteria, number of co-morbidity, use of mechanical ventilation and vasoactive agents, number of non-renal organ failure (NROF), length of ICU stay, and outcomes were recorded. Primary outcome defined as survival at ICU discharge; while secondary outcome as renal recovery (i.e., independence from renal replacement therapy at time of ICU discharge) in survivors.

Continuous variables described as median (25^{th}-75^{th} percentile), and categorical variables are described as n (%). For comparative test on continuous variables, Mann- Whitney U test was applied. For categorical variables, the Pearson Chi- square test or Fisher's exact test were used as appropriate. Logistic regression analysis was used to determine predictors of mortality. Overall, predictors showing a P <0.05 association with ICU mortality in univariate analysis were incorporated in regression analysis. Logistic regression analysis was used to assess the multivariate relation between multiple patient characteristics and outcome of septic AKI. Statistical analysis was done using the SPSS-17 software, $P < 0.05$ was considered significant.

Results

There were 406 patients admitted in ICU during study period. Out of 323 ICU patients with sepsis, 160 patients developed AKI. Of 160, 34 patients were excluded because of any of the following reason: Age <18 years, with end stage renal disease or chronic kidney disease on maintenance hemodialysis, withdrawal of therapy during ICU stay, or incomplete data; and data from medical records of only 126 septic AKI patients were analyzed.

Incidence of septic AKI was 31%. Out of 126 septic AKI patients 75% were male; 85% were medical *vs*. 15% surgical. Primary source of sepsis was lung (40%), followed by intra-abdominal infection (24%), CNS (13%), BSI (8%), UTI (7%), and other/unknown (8%). AKI distribution of these patients in respect of RIFLE criteria were: Risk group 24%, injury group 34%, and failure group 42%. Patients with no NROF were 3%, with one NROF 6%, with two 19%, with three 32%, while with four or more NROF were 40% of total patients. Overall mortality was 52% among patients with septic AKI. Comparison of clinical characteristics among non-survivors (n = 66) and survivors (n = 60) were: Mean age 55 ± 15 *vs*. 49 ± 15 ($P < 0.05$), gender (M: F) 52: 14 *vs*. 42: 18 (NS), APACHE II 24.53 ± 6 *vs*. 18.3 ± 7.8 ($P < 0.05$), number of NROF 4.47 ± 0.7 *vs*. 3.45 ± 1.13 ($P < 0.05$), number of co-morbid illness 2.59 ± 1.1 vs. 2.4 ± 1.14 (NS), length of ICU stay 16 *vs*. 28 days ($P < 0.05$) [Table 1]. Outcome based on RIFLE criteria among non-survivors *vs*. survivors (in %) were: Risk group 40 *vs*. 60; injury group 54 *vs*. 46; and in failure group 58 *vs*. 42.

Age, number of NROF, and APACHE II score were significant predictor of outcome on univariate logistic regression analysis; while number of NROF was found

Table 1: Characteristics of ICU patients with septic AKI

	Non-survivor (n=66)	Survivor (n=60)	P value
Age	55±15	49±15	0.035
Gender (M:F)	52: 14	42: 18	NS
APACHE II score	24.53±6.06	18.3±7.85	0.001
NROF	4.47±0.79	3.45±1.13	0.001
Number of co-morbidity	2.59±1.1	2.4±1.14	0.339
DM *vs*. Non DM	25: 41	23: 37	0.05
LOS in ICU	16	28	0.013

APACHE II: Acute physiological and chronic health evaluation II score; DM: Type 2 diabetes mellitus; LOS: Length of stay; NROF: Non-renal organ failure; ICU: Intensive care unit; AKI: Acute kidney injury

only significant predictor on multivariate logistic regression analysis [Tables 2 and 3]. Relative risk of mortality with individual organ failure was highest with involvement of CVS system (14.5), followed by respiratory failure (9.7), GIT failure (6.2), DIC (3.1), and CNS (2.1) [Table 4]. Renal outcome in survivors at time of ICU discharge were: Dialysis-independent 88% *vs*. dialysis-dependent 12% only. Based on RIFLE criteria, renal recovery in patients with risk and injury group was complete (100%), while in failure group, it was 68%.

Discussion

Both sepsis and AKI are major concern in critically ill patients. Acute kidney injury occurs in about 11-65% of severe sepsis.[15,16] Overall incidence of septic AKI among all ICU admissions is between 15%-20%.[6] In a large multinational, multicenter (no data from Indian subcontinent) prospective study of acute kidney injury in critically ill patients (BEST Kidney investigators), it was found that the most common cause of AKI in ICU patients is sepsis (47.5%).[4] In their study, clinical characteristics of patients were: Mean age 63 years, 60% medical patients, 85% patients required mechanical ventilation, and mean length of stay in ICU was 16 days; while in our study, these were 52 years, 85%, 90%, and 22 days, respectively.

In another large analysis of 14,039 septic AKI patients from Australian ICUs by Bagshaw *et al*., the proportion of patients stratified by RIFLE criteria were 38.5%, 38.8%, and 22.7% for risk, injury, and failure, respectively.[17] In our study, incidence of septic AKI was high at 31% with more proportion of patients in the failure group (24%, 34%, and 42% for risk, injury, and failure, respectively). This is probably explained by the fact that the study cohort was in a referral hospital.

Overall mortality among patients with septic AKI was found to be 70% by BEST Kidney investigators, and prognostic factors were age, severity of illness, use of vasoactive drugs, and mechanical ventilation.[4] In contrast, in our study, the overall mortality was 52% and number of non-renal organ failure, age, and APACHE II score were found to be predictors of outcome in septic AKI patients. In our study, RIFLE criteria did not reveal significant difference for mortality among the 3 grades, but there was a trend of increasing mortality with the severity of AKI increasing from risk to failure. However, RIFLE criteria was found to be a good predictor of recovery of renal function.

This study did not compare septic and non-septic AKI groups. The time of development of AKI in septic patient in relation to ICU admission was also not defined in this study while it is evident by other studies that early septic AKI is not only more common but also shows a trend toward higher mortality. In this study, the mode, intensity, and timing of renal replacement therapy were not analyzed. There is no follow up data of survivors after ICU discharge.

Table 2: Predictors of mortality by univariate logistic regression analysis among patients with septic AKI

Independent variable	Odd ratio	*P* value
Age	0.975	0.038
Gender	0.628	0.26
Number of NROF	0.32	0.001
APACHE II	0.87	0.001
RIFLE	0.65	0.174
Co-morbidity	0.86	0.336
DM	0.99	0.88
Med/Surg	0.69	0.46
Vasoactive drugs	-	0.70
Mechanical ventilation	-	0.71

APACHE II: Acute physiological and chronic health evaluation II score; DM: Type 2 diabetes mellitus; NROF: Non-renal organ failure; AKI: Acute kidney injury; RIFLE: risk, injury, failure, i.e. severity of acute kidney injury

Table 3: Predictors of mortality by multivariate logistic regression analysis among patients with septic AKI

Independent variable	β coefficient	*P* value
Age	0.97	0.08
Number of NROF	0.38	0.001
APACHE II score	0.97	0.08

APACHE II: Acute physiological and chronic health evaluation II score; NROF: Non-renal organ failure; AKI: Acute kidney injury

Table 4: Relative risk of mortality with individual organ failure in patients with septic AKI

Organ failure	Risk ratio	95% CI	*P* value
CVS	14.5	4.6-44.9	0.001
RESP	9.7	2.12-44.9	0.001
GIT	6.29	2.2-17.8	0.001
DIC	3.1	1.4-6.9	0.003
CNS	2.14	1.05-4.37	0.04
HEPATIC	1.7	0.86-3.6	0.08

CVS: Cardiovascular system; RESP: Respiratory system; GIT: Gastrointestinal system; DIC: Disseminated intravascular coagulation; CNS: Central nervous system; AKI: Acute kidney injury; HEPATIC: Liver; CI: Confidence interval

Conclusions

In this cohort of Indian patients septic AKI was found to have a high incidence and mortality. Age, severity of illness as assessed by number of non-renal organ failure and APACHE II score were important predictors of mortality. The number of non-renal organ failure was also found to be an independent predictor of outcome. The RIFLE criteria reliably predicted outcome among survivors but not among non-survivors.

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